

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 12264 - 40	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2005/004872	International filing date (day/month/year) 10/02/2005	(Earliest) Priority Date (day/month/year) 10/02/2004
Applicant PURDUE RESEARCH FOUNDATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. Certain claims were found unsearchable (See Box II).

3. Unity of invention is lacking (see Box III).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____

- as suggested by the applicant.
- as selected by this Authority, because the applicant failed to suggest a figure.
- as selected by this Authority, because this figure better characterizes the invention.

- b. none of the figures is to be published with the abstract.

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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07F13/00 A61K51/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BERRY, NEIL G. ET AL: "Heteroditopic transition metal dithiocarbamate receptors for binding cation-anion ion pairs" XP002332544 retrieved from STN Database accession no. 2003:732428 abstract & JOURNAL OF SUPRAMOLECULAR CHEMISTRY , VOLUME DATE 2002, 2(1-3), 89-92 CODEN: JSCOC9; ISSN: 1472-7862, 2003,</p> <p>-----</p> <p style="text-align: center;">-/--</p>	43

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 July 2005	18.10.2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Richter, H

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; GRANELL, JAUME ET AL: "Studies on the synthesis and electrochemistry of crown ether dithiocarbamates and the molecular dynamics of bis(aza-15-crown- 5)thiuram disulfide. Crystal structure of cobalt tris'(aza-15-crown-5)dithiocarbamate!" XP002332545 retrieved from STN Database accession no. 1990:490225 abstract	43
X	& JOURNAL OF THE CHEMICAL SOCIETY, DALTON TRANSACTIONS: INORGANIC CHEMISTRY (1972-1999), (2), 605-14 CODEN: JCDTBI; ISSN: 0300-9246, 1990, cited in the application	43
A	-& DATABASE BEILSTEIN 'Online! BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; 23 October 1991 (1991-10-23), XP002332644 Database accession no. BRN 3580252; BRN3582715 abstract	49
A	US 6 322 771 B1 (LINDEN JOEL M ET AL) 27 November 2001 (2001-11-27) example 18	1
A	SCHRAMM D ET AL: "SYNTHESIS OF CATIONIC HYDROTRIS(PYRAZOLYL)BORATE ZIRCONIUM COMPOUNDS" INTERNATIONAL CONFERENCE ON ORGANOMETALLIC CHEMISTRY. BOOK OF ABSTRACTS, 16 August 1998 (1998-08-16), page A150, XP002249590	42
A	DIAZ ET AL.: "Interactions of nitric oxide with copper (II) dithiocarbamates in aqueous solution" JOURNAL OF INORGANIC BIOCHEMISTRY, no. 95, 2003, pages 283-290, XP002335489 Scheme 1 page 288	43, 48
A	CAMERON, B ET AL.: "Ruthenium (III) Triazacyclononane Dithiocarbamate..." INORGANIC CHEMISTRY, vol. 42, no. 13, 2003, pages 4102-4108, XP002335490 the whole document	43, 48
		-/-

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category ?	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	VÖGTLE, FRITZ, NEUMANN, PETER: "Stereochemie im Innern cyclischer Verbindungen: Kronenäther, Katapinate und Kryptate" CHEMIKER-ZEITUNG, vol. 97, no. 11, 1973, pages 600-610, XP002335491 -7.-Anwendungen und Ausblick; footnotes 139 and 43 page 608, column 2 -----	49

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1AP20 Rec'd PCT/PTO 02 AUG 2005

International application No.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

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- D1: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BERRY, NEIL G. ET AL: "Heteroditopic transition metal dithiocarbamate receptors for binding cation-anion ion pairs" XP002332544 retrieved from STN Database accession no. 2003:732428
- D2: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; GRANELL, JAUME ET AL: "Studies on the synthesis and electrochemistry of crown ether dithiocarbamates and the molecular dynamics of bis(aza-15-crown-5)thiuram disulfide. Crystal structure of cobalt tris[(aza-15-crown-5)dithiocarbamate]" XP002332545 retrieved from STN Database accession no. 1990:490225
- D3: US-B1-6 322 771 (LINDEN JOEL M ET AL) 27 November 2001 (2001-11-27)
- D4: VÖGTLE, FRITZ, NEUMANN, PETER: "Stereochemie im Innern cyclischer Verbindungen: Kronenäther, Katapinate und Kryptate" CHEMIKER-ZEITUNG, vol. 97, no. 11, 1973, pages 600-610, XP002335491

Invention 1.1

Claim 43 lacks novelty over D1 and D2; see item IV, above.

Invention 1.

Document D3 (example 18), which is considered to represent the most relevant state of the art, discloses ^{99m}Tc -N-Noet (the references in parentheses applying to this document):

From this, the subject-matter of independent claims 1 and 44 differ in the presence of a crown ether.

The subject-matter of claims 1, 44 and 48 is therefore novel (Article 33(2) PCT) The problem to be solved by the present invention may be regarded as the design of new

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radiotracers for myocardial perfusion imaging.

The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) because crown ether groups allow faster clearance of the ^{99m}Tc -nitrido complexes from liver and lungs and better heart/liver and heart/lung ratios; see the description, paragraph [00151]. This property of crown ethers is not described in one of the available documents.

Claims 2-42 and 45-47 are dependent on claim 1 or 44 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

Claim 48 is inventive because the use as NO or reactive oxygen species scavengers of dithiocarbamates of the structure defined in claim 48 have not yet been suggested in a therapy of a disease resulting from overproduction of nitric oxide or reactive oxygen species; see paragraphs [00162] to [00164] and the documents J. Inorg. Biochem. 2003, 95, 293 and Inorg. Chem. 2003, 42, 4102.

None of the available documents describes the use of crowned dithiocarbamates according to claim 49.

Medical applications of crown ethers for metal removal are suggested in D4, section 7; see "Entkalkungen" in line 7 from the bottom. Yet there is no connection of D4 to dithiocarbamates.

Claim 49, therefore, is novel and inventive.

Re Item VII.

Additional reasons that the application does not meet the requirements of the PCT are as follows:

The obscure statement on 68, paragraph [00235] or at least the reference to the equivalents should be removed because it is an attempt to change the scope of the claims

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in an unclear and undefined way (Art. 6, EPC)

If the applicants wish to incorporate the document mentioned in the first paragraph the disclosure thereof should be included expressis verbis in the description or the partial phrase "incorporated by reference" should be deleted. Thereby, where present, application serial numbers should be replaced by publication numbers.

Re Item VIII.

The application does not meet the requirements of Article 6 PCT, because claim 43 is not clear.

The trivial solution $p=0 p'=0$ also comprised by claim 43 has not been searched and should be removed. Furthermore, the definition R14 seems to be superfluous.